Reviewer's report

Title: Delayed-onset of progressive pseudorheumatoid dysplasia in a Chinese adult with a novel compound WISP3 mutation: a case report

Version: 0 Date: 23 Sep 2017

Reviewer: Susana Balcells

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MGTC-D-17-0021 "A delayed-onset of progressive pseudorheumatoid dysplasia …" by Hu et al.

The MS describes one case of atypical (late-onset) male pseudo rheumatoid dysplasia (PPD) from China. The case had been misdiagnosed as congenital spondyloepiphyseal dysplasia at age 15 and left without a therapy. Twenty years later, with a history of pain, mobility limitation in many joints and overall worsening, the patient was rediagnosed as ankylosing spondylitis and referred to Ruijin Hospital (Shanghai) where a detailed clinical reevaluation strongly suggested a diagnosis of PPD. This was confirmed with genetic testing of the patient, his parents and his son. The patient was a compound heterozygote for 1 previously described nonsense mutation and a novel frameshift mutation in the causative gene (WISP3). Counseling could be given for his son (a carrier of just one of the 2 mutations, thus non affected).

The interesting points of the MS are the description of Chinese PPD mutations (so far, few of them have been reported) and the atypical late-onset presentation of PPD in the patient.

General Comments

Awkward English and use of genetic terminology, that need amendment before the paper can be published. The current recommendations of HGVS for mutation nomenclature (to use the 3 letter abbreviation for amino acids, rather the one letter one) are not followed in the MS.

Given the atypical late-onset disease of the patient, a discussion of the possible genotype-phenotype correlations for the mutation that has been previously described (by comparing this patient and the other carrier/s) is missing.

A comprehensive discussion of the Chinese mutations and genotypes published so far and the corresponding phenotypes would add value to the MS.
Some of the mistakes

Page 2 line 5: "pseudorheumatoid dysplasia" (should read "pseudorheumatoid dysplasia")

Page 2 line 24-29: "a novel compound WISP3 mutation in exon 4, a frameshift mutation … and a nonsense mutation …" (should read "two WISP3 mutations in exon 4, a novel frameshift mutation … and an already described nonsense mutation")

Page 2 line 34: "..we identified that the son …" should read: "..we identified that the proband's son …"

Page 3 line 3: the MIM number is incorrect. It reads MIM208032 (should read MIM208230).

Page 5 line 22: "parental" should be replaced by "paternal"

Page 5 line 37: "infected" should read "affected".

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

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